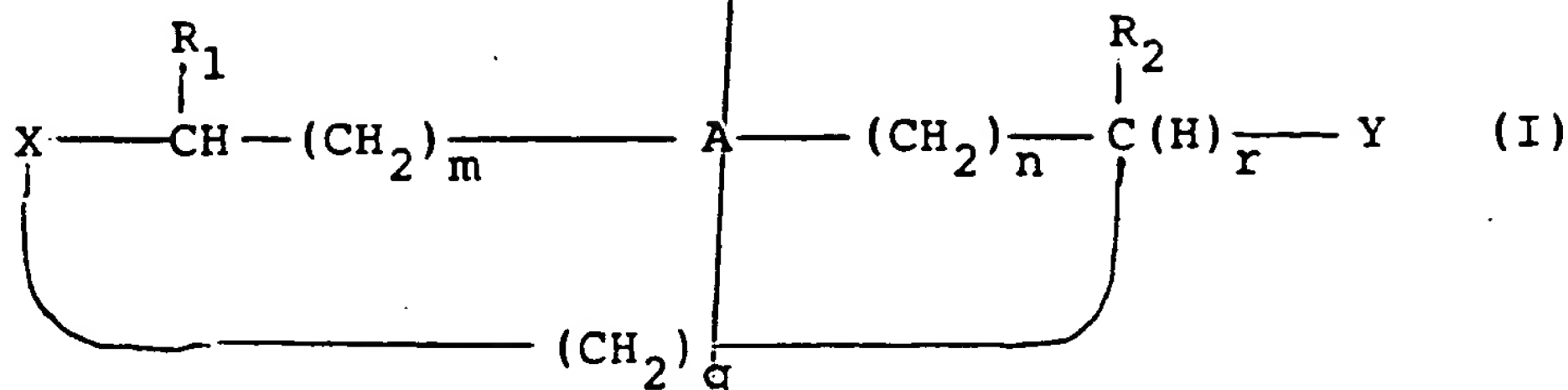


WE CLAIM:

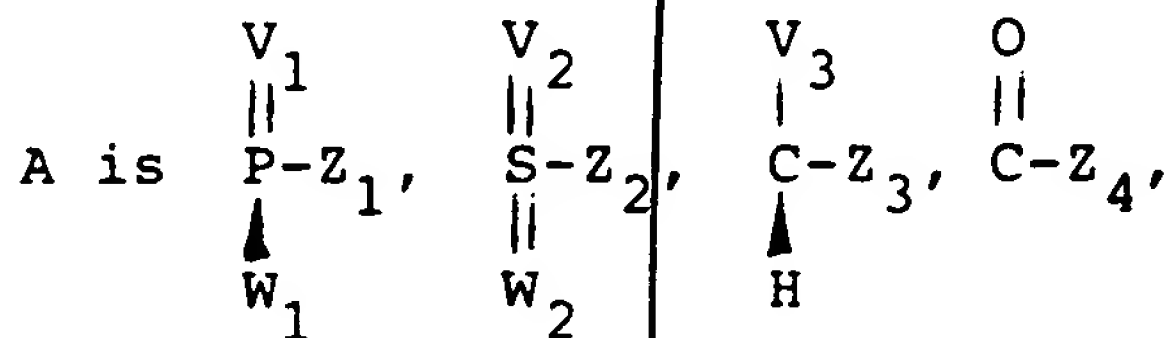
1. A hapten of formula I

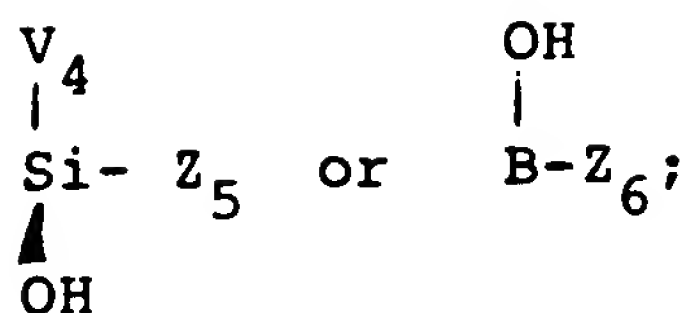


wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, or (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CH<sub>2</sub>CH(CO<sub>2</sub>H)<sub>2</sub>, -(CH<sub>2</sub>)<sub>2</sub>S(O)CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>S(O)<sub>2</sub>CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>3</sub>ONHC(=NH)NH<sub>2</sub>;

m, n and q may be the same or different and each is 0 or an integer from 1 to 10 and r is 0 or 1 provided that if r is 1, then there is no bond between X and the carbon bonded to R<sub>2</sub>;





$V_1$  is O or S;

$V_2$  is O or a lone pair of electrons;

$V_3$  and  $V_4$  are OH or  $\text{NH}_2$ ;

$W_1$  is OH,  $\text{NH}_2$ , SH or H;

$W_2$  is O or a lone pair of electrons;

X is hydrogen, oxygen, amino, amino protected by a protecting group selected from the group consisting of terminal amino protecting groups, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, said amino acid and peptide being unprotected or protected by said protecting group, or X is alkene,  $(\text{C}_1-\text{C}_9)$ alkyl,  $(\text{C}_1-\text{C}_9)$ alkoxy, phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen,  $(\text{C}_1-\text{C}_4)$ alkyl,  $(\text{C}_1-\text{C}_4)$ alkoxy or  $(\text{C}_1-\text{C}_4)$ alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a protecting group selected from the group consisting of terminal carboxyl protecting groups, a carbonyl bonded to the N terminus of a naturally occurring amino acid to form a peptide bond, carbonyl bonded to the N terminus of a peptide to form a peptide bond, said amino acid and peptide being

protected or unprotected by said protecting group, or Y is (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-C<sub>9</sub>)alkoxy, phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl; and wherein

each of said substituents R<sub>1</sub>, R<sub>2</sub>, X and Y may be unbound or bound to one or more of said remaining substituents R<sub>1</sub>, R<sub>2</sub>, X and Y and if bound, then by a covalent bond or a linker moiety selected from the group consisting of -(CH<sub>2</sub>)<sub>s</sub>-S-S-(CH<sub>2</sub>)<sub>t</sub>-, -(CH<sub>2</sub>)<sub>t</sub>-, -S-(CH<sub>2</sub>)<sub>t</sub>-S-, -(CH<sub>2</sub>)<sub>s</sub>-S-(CH<sub>2</sub>)<sub>t</sub>-, -(CH<sub>2</sub>)<sub>s</sub>-CH=CH-(CH<sub>2</sub>)<sub>t</sub>-, -(CH<sub>2</sub>)<sub>s</sub>-NH-CO-(CH<sub>2</sub>)<sub>t</sub>-, -(CH<sub>2</sub>)<sub>s</sub>-NH-(CH<sub>2</sub>)<sub>t</sub>- and -(CH<sub>2</sub>)<sub>s</sub>-Ø-(CH<sub>2</sub>)<sub>t</sub>-;

Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> and Z<sub>6</sub> may be unbound or bound to said linker moiety; and if unbound Z<sub>1</sub> is O, NH, CH<sub>2</sub> or S, Z<sub>2</sub> is O, NH or CH<sub>2</sub>, Z<sub>3</sub> is CH<sub>2</sub>, Z<sub>4</sub> is CF<sub>2</sub> or CF<sub>2</sub>CO and Z<sub>5</sub> and Z<sub>6</sub> are O or CH<sub>2</sub> provided that if Z<sub>1</sub> is O or NH and if V<sub>1</sub> is O and if W<sub>1</sub> is OH, then r is either 0 or r is 1 and at least one of said substituents R<sub>1</sub>, R<sub>2</sub>, X or Y is bound to one or more of said remaining substituents R<sub>1</sub>, R<sub>2</sub>, X and Y and further provided that if Z<sub>3</sub> is CH<sub>2</sub> and if V<sub>3</sub> is OH, then r is either 0 or r is 1 and at least one of said substituents R<sub>1</sub>, R<sub>2</sub>, X or Y is bound to one or more of said remaining substituents R<sub>1</sub>, R<sub>2</sub>, X and Y; and if bound Z<sub>1</sub> and Z<sub>2</sub> are N or CH, Z<sub>4</sub> is CF or CFCO and Z<sub>3</sub>, Z<sub>5</sub> and Z<sub>6</sub> are CH and further provided that if Z<sub>1</sub>, Z<sub>2</sub>,

$Z_3, Z_4, Z_5$  or  $Z_6$  is bound to said linker moiety, it is covalently bound to said linker moiety by substitution at an appropriate atom of said linker moiety; and

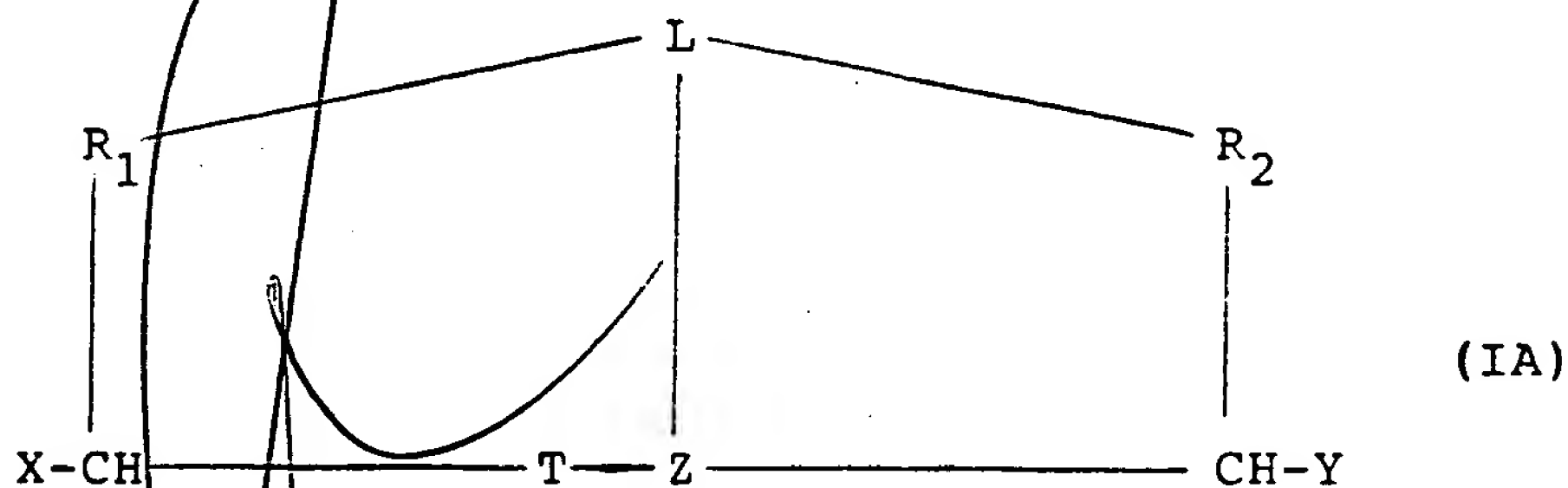
s and t may be the same or different and each is 0 or an integer from 1 to 10 unless the linker moiety is  $-(CH_2)_t-$  in which case t is an integer from 1 to 10.

2. An immunogen capable of eliciting a catalytic antibody comprising:

(a) a hapten of formula I as claimed in claim 1; and

(b) a suitable carrier molecule.

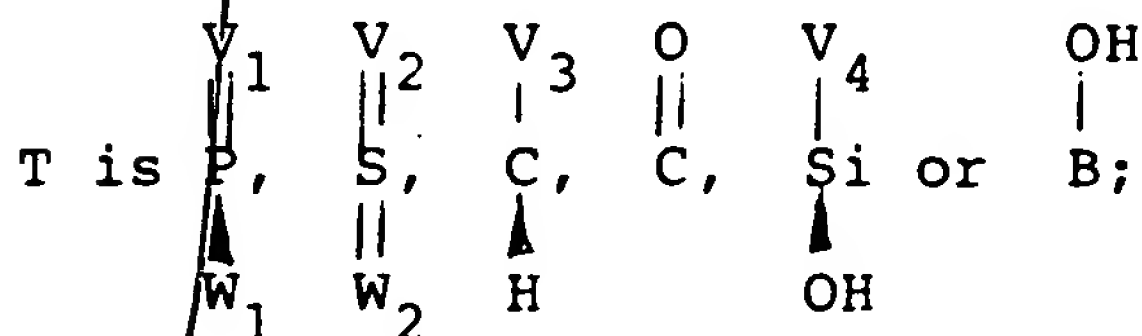
3. A hapten of claim 1 having formula IA



wherein

$R_1, R_2, X$  and  $Y$  and are as defined in

claim 1;



$V_1, V_2, V_3, V_4, W_1$  and  $W_2$  are as defined in claim 1;

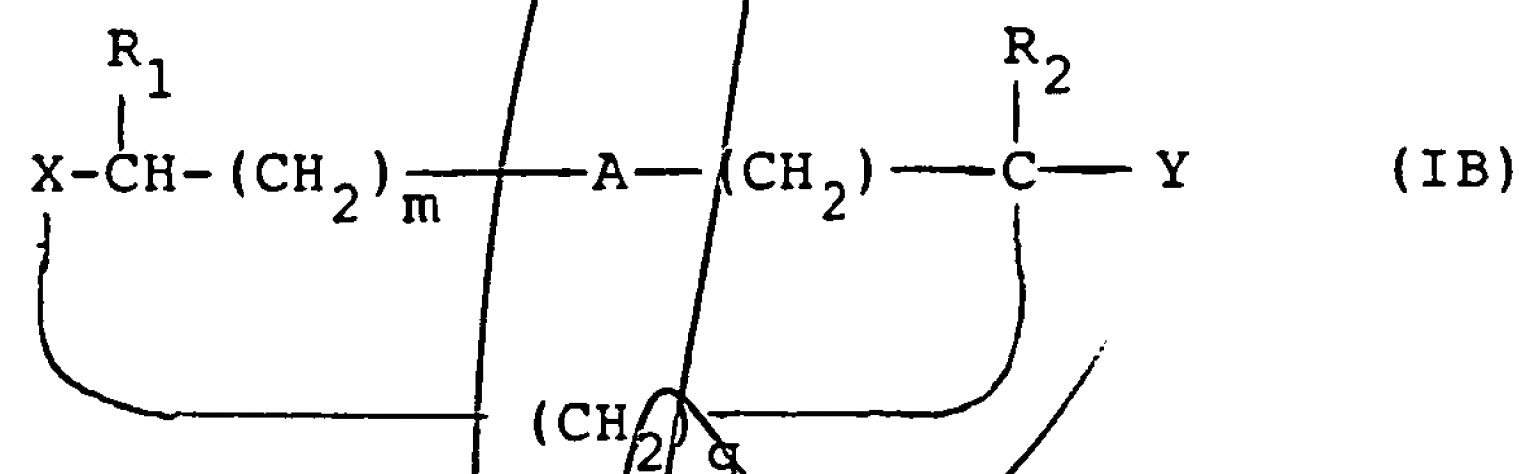
$Z$  is  $Z_1, Z_2, Z_3, Z_4, Z_5$  or  $Z_6$  as defined in claim 1;

and

$L$  is  $N$  or  $CH$  in the linker moiety as defined in claim 1.

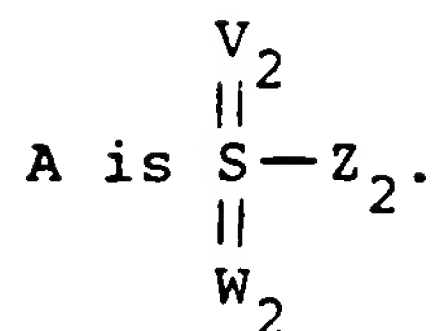
4. The hapten of claim 3 wherein in formula IA,  $R_1$  and  $R_2$  are  $-CH_2-$  or  $-CH_2CH_2-$  and the linker moiety is  $-CH_2-CO-N-CH_2-$ ,  $-CH_2-N-CH_2-$ ,  $-CH_2-CH-S-$  or  $-ortho-phenyl-CH-CH_2-$ .

5. A hapten of claim 1 having formula IB,



wherein  $R_1, R_2, X, Y, A, m, n$  and  $q$  are defined as in claim 1.

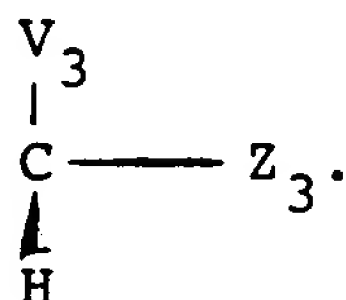
6. A hapten of claim 1 wherein formula I,



7. A hapten of claim 6 wherein  $V_2$  and  $W_2$  are O and  $Z_2$  is NH.

8. The hapten of claim 7 which is aminomethanesulfonamidylalanyl acid.

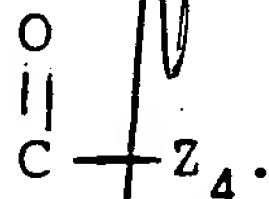
9. A hapten of claim 1 wherein formula I, A is



10. A hapten of claim 9 wherein  $V_3$  is OH and  $Z_3$  is  $CH_2$ .

11. A hapten of claim 9 wherein  $V_3$  is  $NH_2$  and  $Z_3$  is  $CH_2$ .

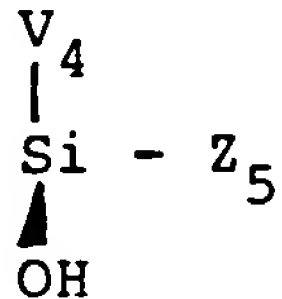
12. A hapten of claim 1 wherein A is



13. A hapten of claim 12 wherein  $Z_4$  is  $CF_2$ .

14. The hapten of claim 13 which is  
5-(serinyl)amino 3, 3 difluoro 4-oxo 6-hydroxy heptanoic acid.

15. The hapten of claim 1 wherein A is

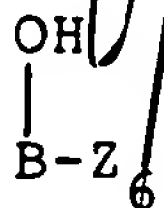


16. A hapten of claim 15 wherein  $V_4$  is OH and  $Z_5$  is  
O.

17. A hapten of claim 16 wherein  $V_4$  is OH and  $Z_5$  is  
 $CH_2$ .

18. The hapten of claim 17 which is  
3-(aminomethyldihydroxysilyl) propionic acid.

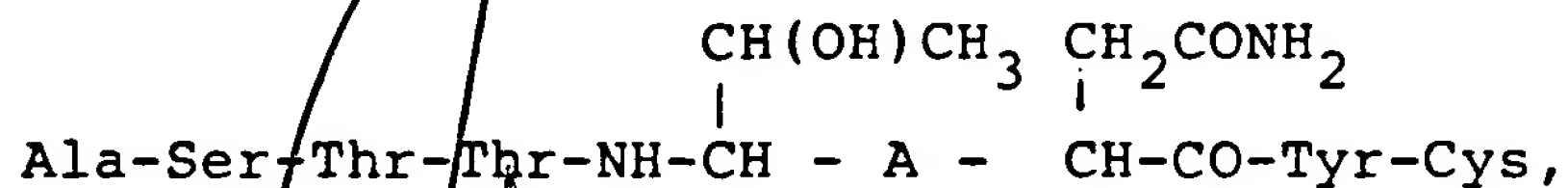
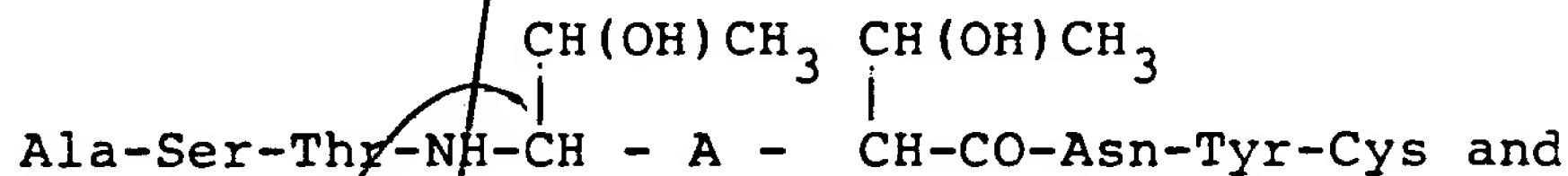
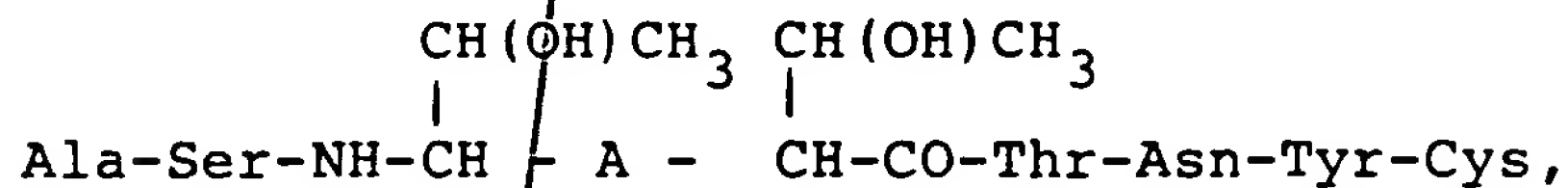
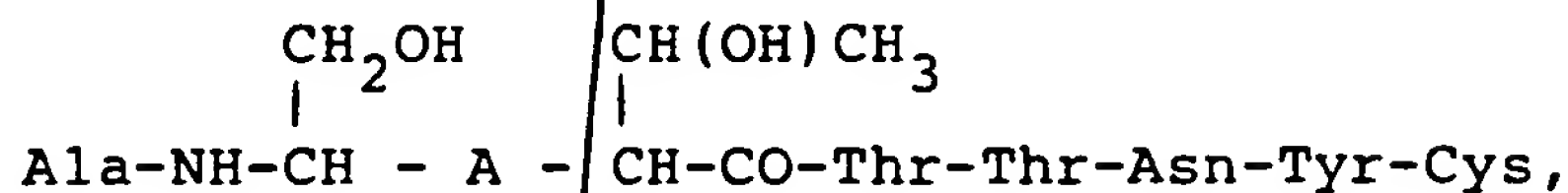
19. A hapten of claim 1 wherein A is



20. A hapten of claim 19 wherein  $Z_6$  is O.

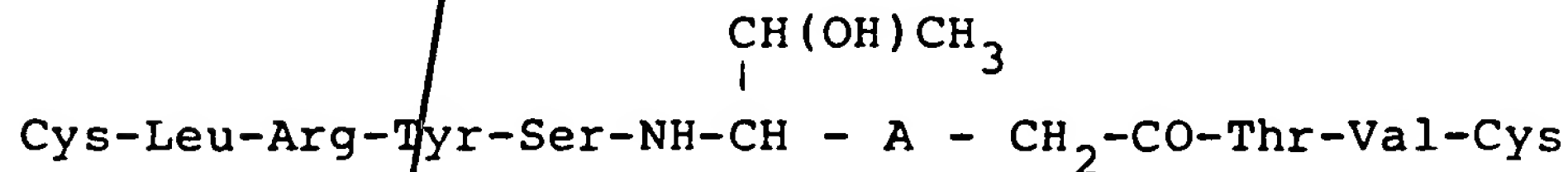
21. The hapten of claim 20 which is  
(S)-lactate-1-(R)-amino-2-phenylethane boronate.

22. A hapten according to claim 1 which is selected  
from the group consisting of



wherein A is as defined in claim 1.

23. A hapten according to claim 1 which is

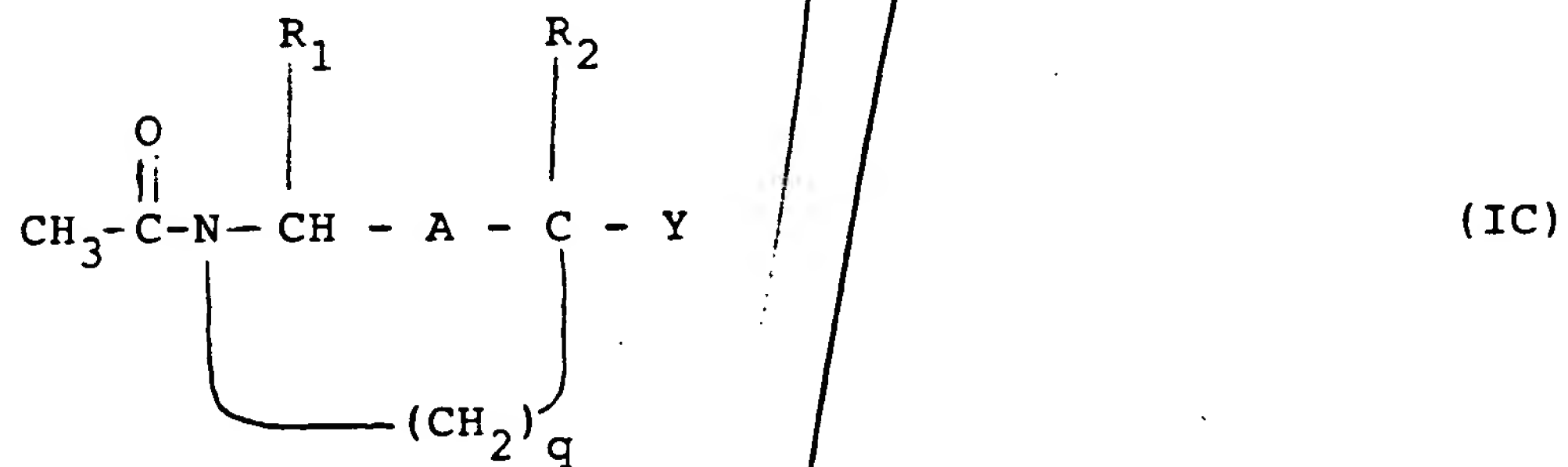


wherein A is as defined in claim 1.



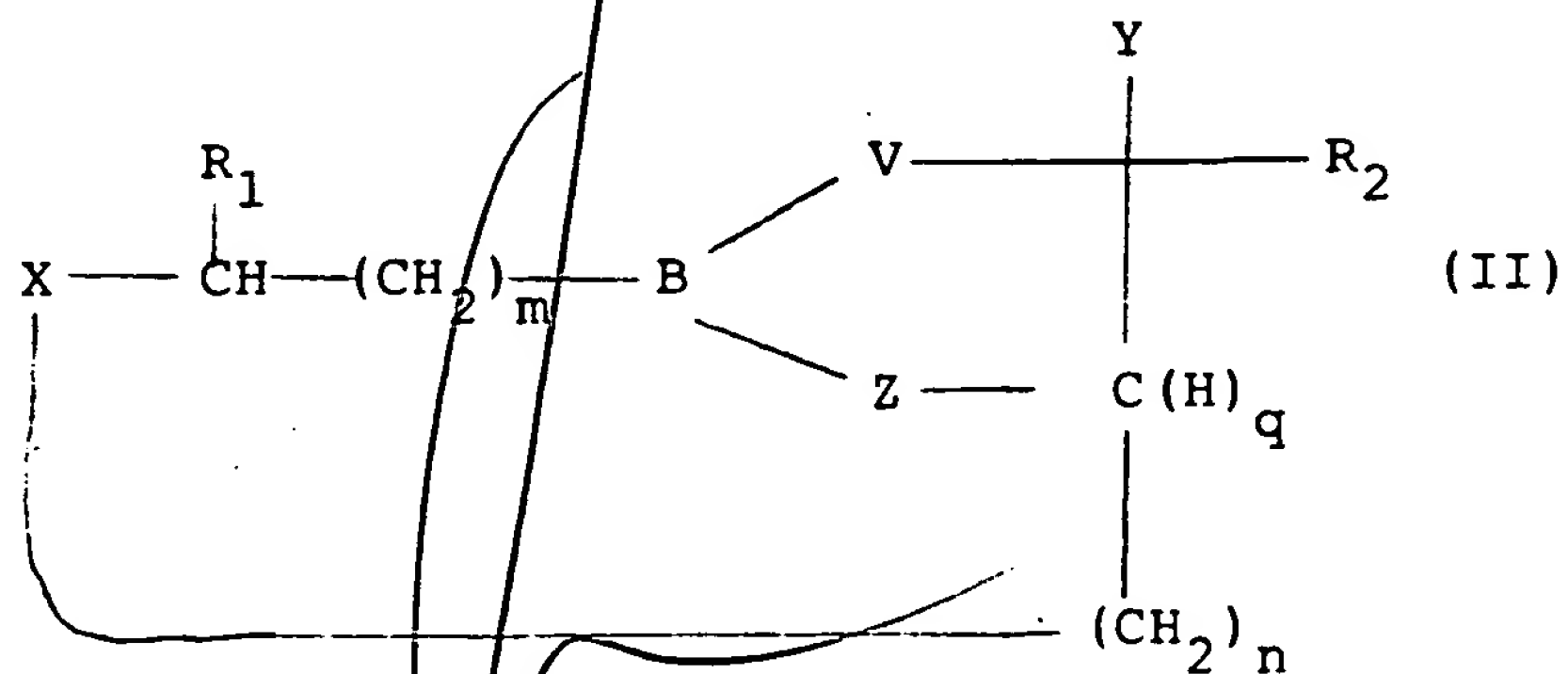
24. A hapten according to claim 23 having a  $\beta$ -turn configuration mimicking the configuration of native protein wherein the sulfur atoms in the two terminal cysteine residues are joined to form a disulphide bridge.

25. A hapten according to claim 5 of formula IC



wherein  $R_1$ ,  $R_2$ , A, Y and q are as defined in claim 5.

26. A boron-containing hapten of formula II



wherein

$R_1$  and  $R_2$  may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated,

phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amino group may be glycosylated or  $(C_1-C_4)$ alkyl,  $-CH_2CH(CO_2H)_2$ ,  $-(CH_2)_2S(O)CH_3$ ,  $-(CH_2)_2S(O)_2CH_3$ ,  $-(CH_2)_3NH_2$  or  $-(CH_2)_3ONHC(=NH)NH_2$ ;

V is O,  $CH_2$  or NH;

X is hydrogen, oxygen, amino, amino protected by a protecting group selected from the group consisting of terminal amino protecting groups, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, said amino acid and peptide being unprotected or protected by said protecting group, or X is alkene,  $(C_1-C_9)$ alkyl,  $(C_1-C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen,  $(C_1-C_4)$ alkoxy or  $(C_1-C_4)$ alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a protecting group selected from the group consisting of terminal carboxyl protecting groups, a carbonyl bonded the N terminus of a naturally occurring amino acid to form a carbonyl bonded to the N terminus of a peptide to form a peptide bond, said amino acid and peptide being protected or unprotected by said protecting group, or Y is  $(C_1-C_9)$ alkyl,  $(C_1-C_9)$ alkoxy, or phenyl phenoxy, cyclohexyl, phenylthio,

B1  
phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl; and wherein

Z is O, CH<sub>2</sub> or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then there is no bond between X and the carbon bond to Z.

27. The haptens of claim 26 wherein m is 0 and q is 2.

28. The hapten of claim 27 which is (R)-2-hydroxymethyl-2-hydroxypropionic acid diol-1-amino-2-phenylethaneboronate.

29. A hapten according to claim 26 wherein  
R<sub>1</sub> is selected from the group consisting of CH<sub>2</sub>OH and CH(OH)CH<sub>3</sub>,  
R<sub>2</sub> is selected from the group consisting of CH(OH)CH<sub>3</sub> and CH<sub>2</sub>CONH<sub>2</sub>,  
X is selected from the group consisting of amino bonded to the C terminus of alanine, amino bonded to the C terminus of serine in the dipeptide Ala-Ser, amino bonded to the C terminus of threonine in the tripeptide

Sub B2

B2  
Ala-Ser-Thr and amino bonded to the C terminus of threonine in the polypeptide Ala-Ser-Thr-Thr and

Y is selected from the group consisting of carbonyl bonded to the N terminus of threonine in the polypeptide Thr-Thr-Asn-Tyr-Cys, carbonyl bonded to the N terminus of threonine in the polypeptide Thr-Asn-Tyr-Cys, carbonyl bonded to the N terminus of asparagine in the tripeptide Asn-Tyr-Cys and carbonyl bonded to the N terminus of tyrosine in the dipeptide Tyr-Cys.

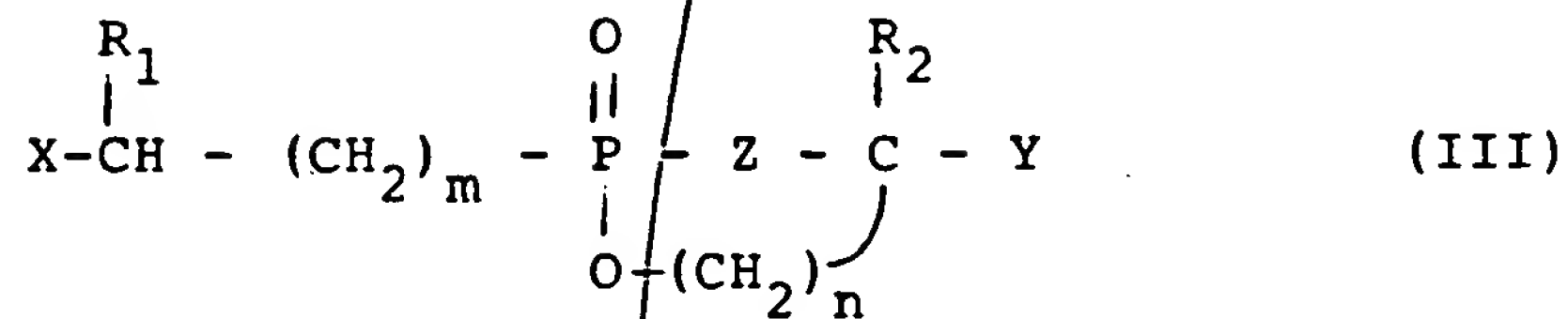
30. A hapten according to claim 26 wherein  $R_1$  is  $\text{CH}(\text{OH})\text{CH}_3$ ,  $R_2$  is H, X is amino bonded to the C terminus of serine in the polypeptide Cys-Leu-Arg-Tyr-Ser and Y is carbonyl bonded to the N terminus of threonine in the tripeptide Thr-Val-Cys.

31. A hapten according to claim 30 having a  $\beta$ -turn configuration mimicking the configuration of native protein wherein the sulfur atoms in the two terminal cysteine residues are joined to form a disulphide bridge.

32. An immunogen capable of eliciting a catalytic antibody comprising:

- Sub B31
- (a) a hapten of formula II as defined in claim 27; and
  - (b) a suitable carrier molecule.

33. A phosphorus containing hapten of formula III



wherein

$\text{R}_1$  and  $\text{R}_2$  may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated or  $(\text{C}_1-\text{C}_4)$ alkyl,  $-\text{CH}_2\text{CH}(\text{CO}_2\text{H})_2$ ,  $-(\text{CH}_2)_2\text{S}(\text{O})\text{CH}_3$ ,  $-(\text{CH}_2)_2\text{S}(\text{O})_2\text{CH}_3$ ,  $-(\text{CH}_2)_3\text{NH}_2$  or  $-(\text{CH}_2)_3\text{ONHC}(=\text{NH})\text{NH}_2$ ;

X is hydrogen, amino, amino protected by a protecting group selected from the group consisting of terminal amino protecting groups, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, said amino acid and peptide being unprotected or protected by said protecting group, or X is alkene,  $(\text{C}_1-\text{C}_9)$ alkyl,  $(\text{C}_1-\text{C}_9)$ alkoxy, or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted

or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl;

63  
Y is hydrogen, carboxyl, carboxyl protected by a protecting group selected from the group consisting of terminal carboxyl protecting groups, a carbonyl bonded to the N terminus of a naturally occurring amino acid to form a peptide bond, carbonyl bonded to the N terminus of a peptide to form a peptide bond, said amino acid and peptide being protected or unprotected by said protecting group, or Y is (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-C<sub>9</sub>)alkoxy, or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl;

Z is O or NH; and

m and n may be the same or different and each is 0 or an integer from 1 to 10.

34. An immunogen capable of eliciting a catalytic antibody comprising:

- (a) a hapten of formula III as defined in claim 33; and
- (b) a suitable carrier molecule.

35. A catalytic antibody elicited by an antigen comprising the hapten of claim 1.

36. A catalytic antibody elicited by an antigen comprising the hapten of claim 26.

37. A catalytic antibody elicited by an antigen comprising the hapten of claim 33.

38. A catalytic antibody which can catalyze a chemical reaction of interest and which is elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 1, said catalytic antibody having been prepared by a process comprising the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

39. A catalytic antibody which can catalyze a chemical reaction of interest and which is elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 26, said catalytic antibody having been prepared by a process comprising the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

40. A catalytic antibody which can catalyze a chemical reaction of interest and which is elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 33, said catalytic antibody having been prepared by a process comprising the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with mecloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.



41. A method for producing catalytic antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 1, wherein said method comprises the steps of:

- (a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;
- (b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and
- (c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

42. A method for producing catalytic antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 26, wherein said method comprises the steps of:

- (a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;
- (b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

BS (c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

43. A method for producing catalytic antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by an antigen comprising the hapten of claim 33, wherein said method comprises the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

44. A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the hapten of claim 1.

45. A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the hapten of claim 26.

46. A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the hapten of claim 33.

47. A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises contacting said molecule with an effective amount of a catalytic antibody elicited with a hapten of claim 1, said hapten having complementarity with said specific amino acid sequence.

48. A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises contacting said molecule with an effective amount of a catalytic antibody elicited with a hapten of claim 26, said hapten having complementarity with said specific amino acid sequence.

49. A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises contacting said molecule with an effective amount of a catalytic antibody elicited with a hapten of claim 33, said hapten having complementarity with said specific amino acid sequence.

50. A method for treating acquired immune deficiency syndrome by inhibiting human immunodeficiency virus which comprises treating a patient with an effective amount of a catalytic antibody elicited using a hapten of claim 22.

51. A method for treating acquired immune deficiency syndrome by inhibiting human immunodeficiency virus which comprises treating a patient with an effective amount of a catalytic antibody elicited using a hapten of claim 29.

52. A method for treating acquired immune deficiency syndrome by inhibiting human immunodeficiency virus which comprises treating a patient with an effective amount of a catalytic antibody elicited using a hapten of claim 33.

53. A method for treating hypertension by inhibiting human renin activity which comprises treating a

patient with an effective amount of a catalytic antibody elicited using a hapten of claim 23.

54. A method for treating hypertension by inhibiting human renin activity which comprises treating a patient with an effective amount of a catalytic antibody elicited using a hapten of claim 30.

55. A method for treating hypertension by inhibiting human renin activity which comprises treating a patient with an effective amount of a catalytic antibody elicited using a hapten of claim 33.

PL33.01